Genetics & the Future of Healthcare

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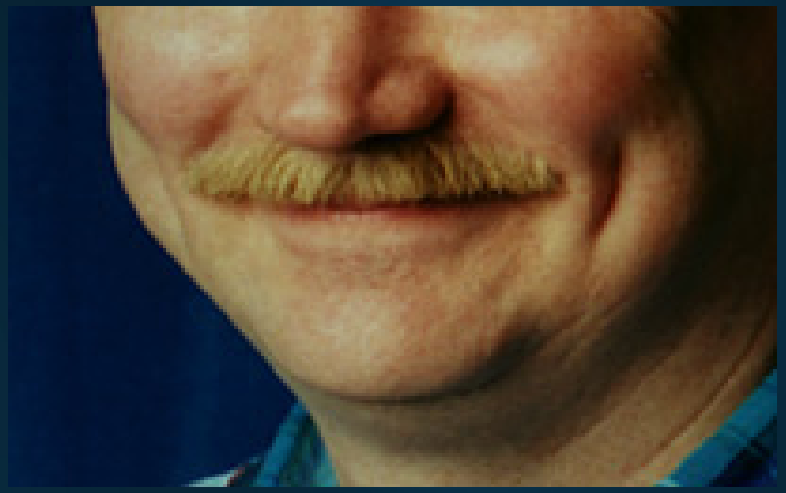
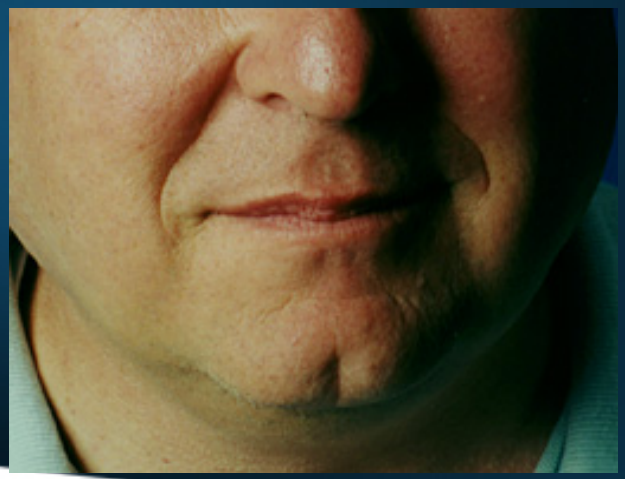
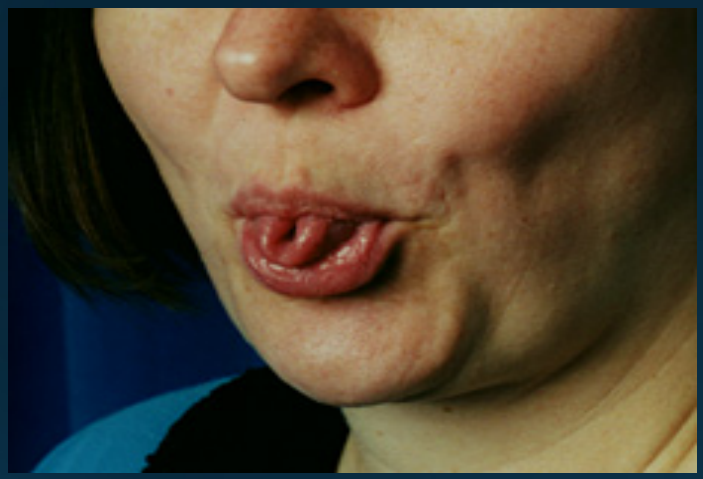
Continuing Education Cruise 2013

Do You Have???







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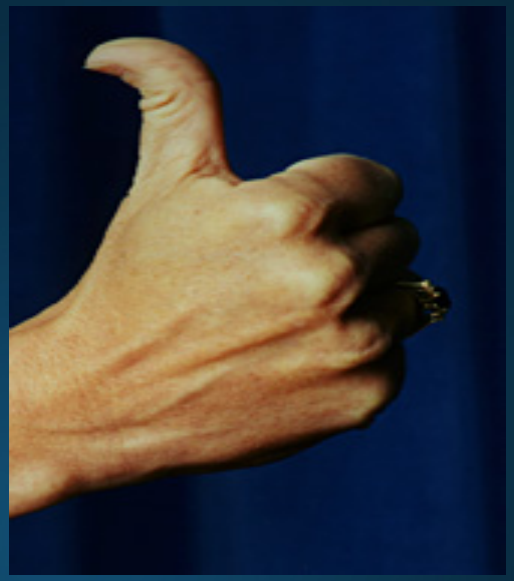

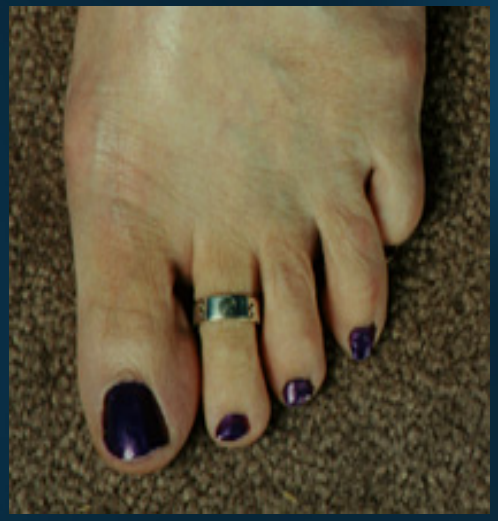

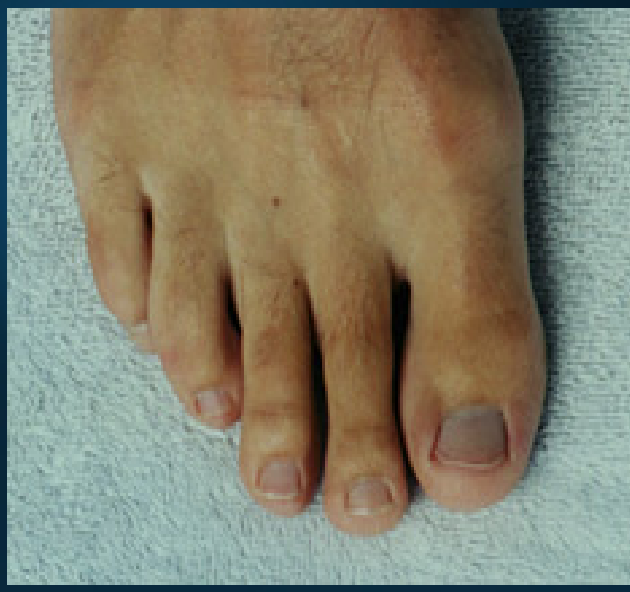

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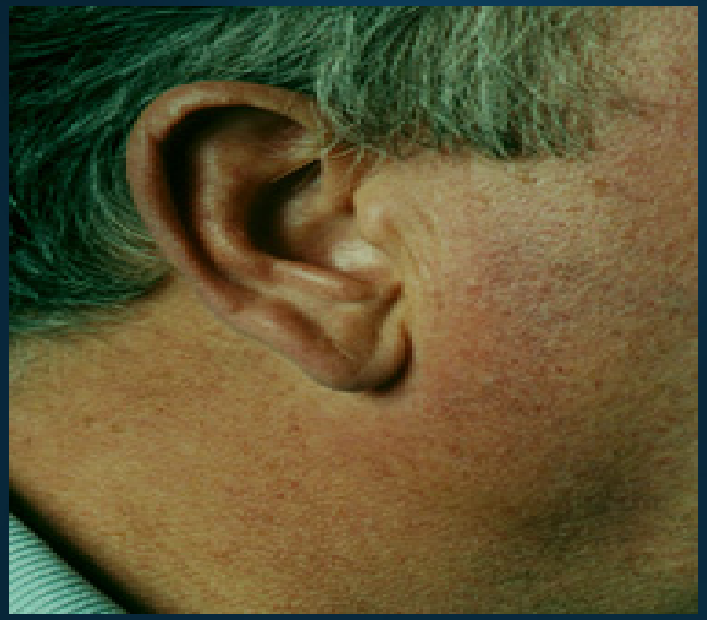


Useless Information That's Fun to Know

- Researchers have discovered that you can tell if someone is right or left-handed literally off the top of your head - by checking which way their hair grow out of their scalp. Right-handed people tend to have hair that swirls clockwise, from the whorl or crown (the place at the back of the head where hair appears to grow in a spiral). People who are left-handed or ambidextrous, however have no such pattern - the hair can coil in either direction.
- Hair swirls

Why do healthcare professionals need to know the mechanics of genetics?

- Recent advances in molecular biology and genetics have revolutionized the health care field by providing the molecular tools needed to determine the genetic component of most diseases.
- A growing number of health care professionals working in this area are offering and interpreting genetic tests to individuals and families.

Why do healthcare professionals need to know the mechanics of genetics?

- Nurses are likely to be the first health care professionals from whom individuals and families seek guidance regarding the complexities of genetic testing and interpretation.
- Nurses may identify a family in need of genetic counseling
- Nurses should provide emotional support during aspects of the counseling process

Roles of the Nurse In Genetics

- Identify individuals with genetic conditions
- Collecting and recording genetics information
- Offer genetics information & assess the client's comprehension of the info
- Obtain necessary consent forms for genetic testing (for minors)
- Assess the family's response to a diagnosis
- Provide care for affected clients
- Recognize risks for discrimination
- Identify and instruct on resources for the family/individual

The Human Genome Project

- This is a publicly funded international project that is coordinated by the National Institutes of Health (NIH) and the U.S. Department of Energy.

- It was initiated in 1990 with **the ultimate goal of mapping the human genome**, which is the complete set of genetic instructions in the nucleus of each human cell.

The Human Genome Project

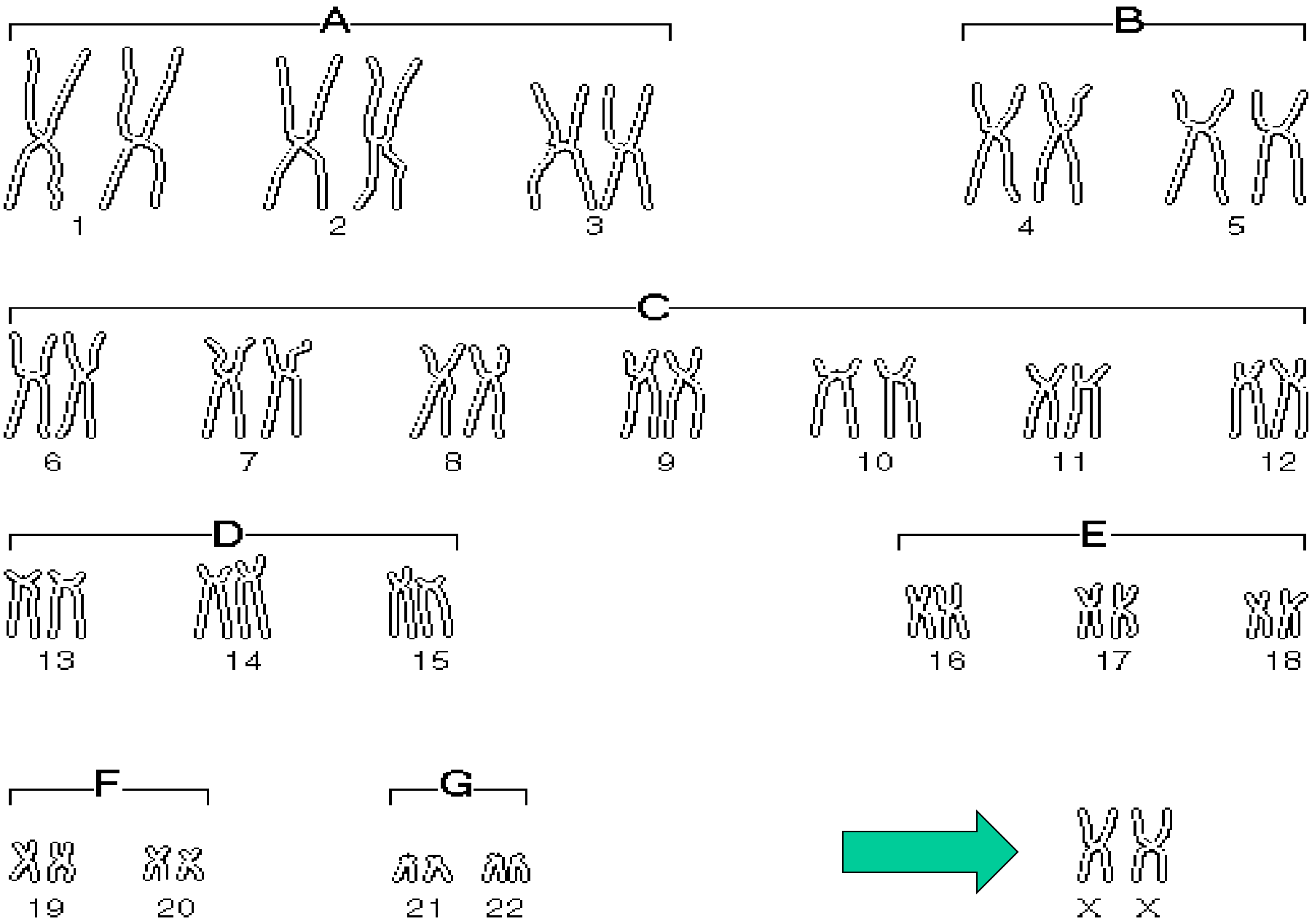
- Initial efforts to sequence and analyze the human genome have produced highly valuable information. For example, more that 100 genes involved in diseases such as heart disease, breast CA, colon CA, Alzheimer disease, cystic fibrosis (CF) and achondroplasia have been identified.

- Genetic tests for more than 700 inherited conditions are commercially available or in research development.

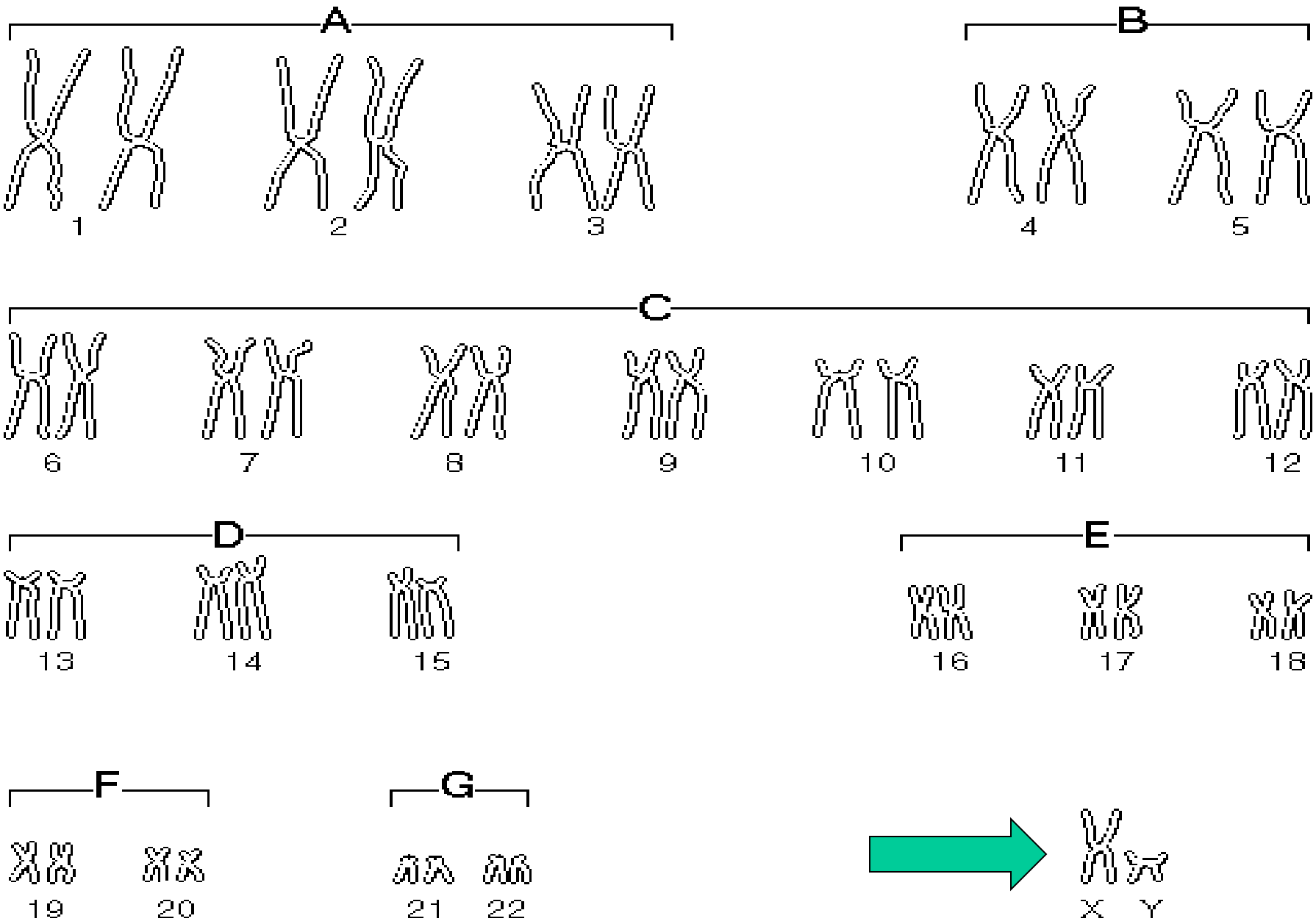
Gene Identification & Testing

- Genetic testing – involves the analysis of human DNA (deoxyribonucleic acid) & RNA (ribonucleic acid).
- Prenatal testing is done to identify the genetic status of a pregnancy at risk for a genetic condition (maternal serum screening). This can be a controversial & ethical test.
- Carrier screening is done to identify individuals who have a gene mutation for a genetic condition but do not show symptoms of the condition (phenotype).

Normal Female Karyotype



Normal Male Karyotype

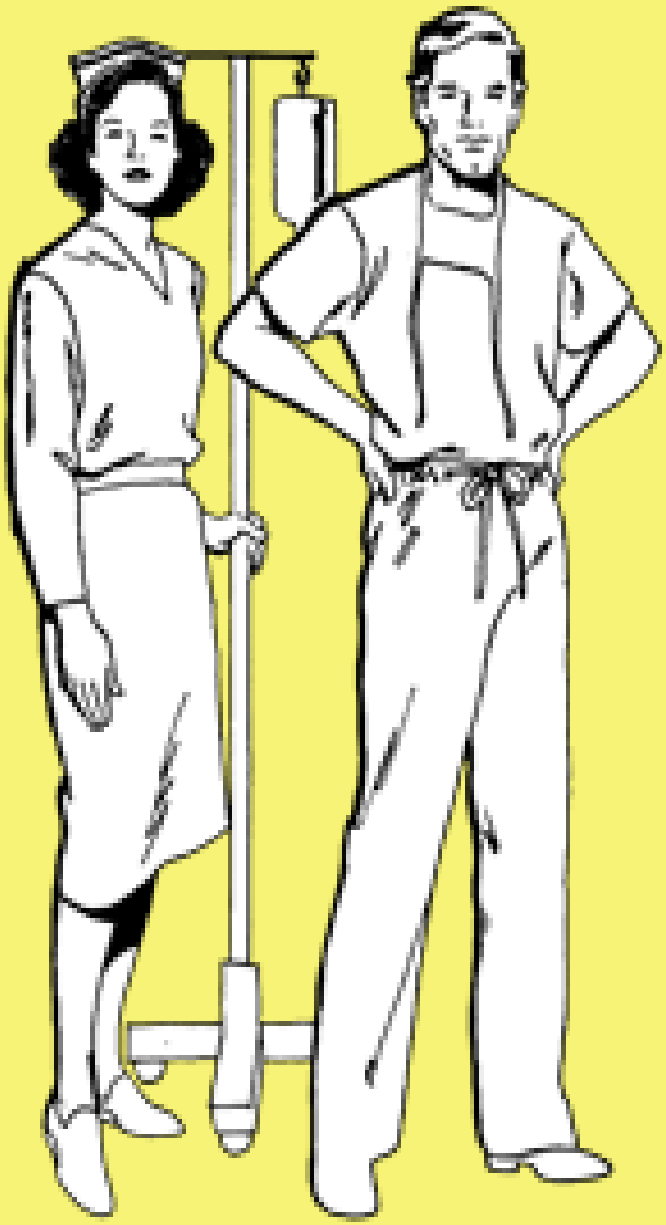


Pharmacogenomics

- Thanks to breakthroughs from the Human Genome Project, we now have pharmacogenomics. This is the use of genetic information to individualize drug therapy. This will likely become part of the future standard practice of determining drug selection for the treatment of diseases that are specific to the client's unique genetic makeup.

Nursing...

A profession where you must also wash your hands BEFORE using the restroom.



someecards
user card

Chronic Diseases with Ongoing Pharmacogentics Research

- Cancer
- Asthma
- HIV Infection
- Hypertension
- Diabetes
- Heart Failure
- Hyperlipidemia
- Coagulation Disorders
- Alzheimer's Disease
- Psychiatric Disorders
- Hormone Replacement

Gene Therapy

- This includes targeting the right gene at the right location in the right cells, expressing the transferred gene at the right time, and minimizing adverse reactions. The goal here is to provide cures for many devastating diseases via gene therapy.

Ethical, Legal, and Social Implications (ELSIs) of Genetic Testing

- A major risk associated with genetic testing is gaining information that may result in increased anxiety and altered family relationships. The affected individual or family may endure discrimination.

- Also, the tests are not 100% accurate, which could result in false-negative or false-positive results. Thus, resulting in unnecessary treatments, or the lack of necessary treatments.

Ethical, Legal, and Social Implications (ELSIs) of Genetic Testing

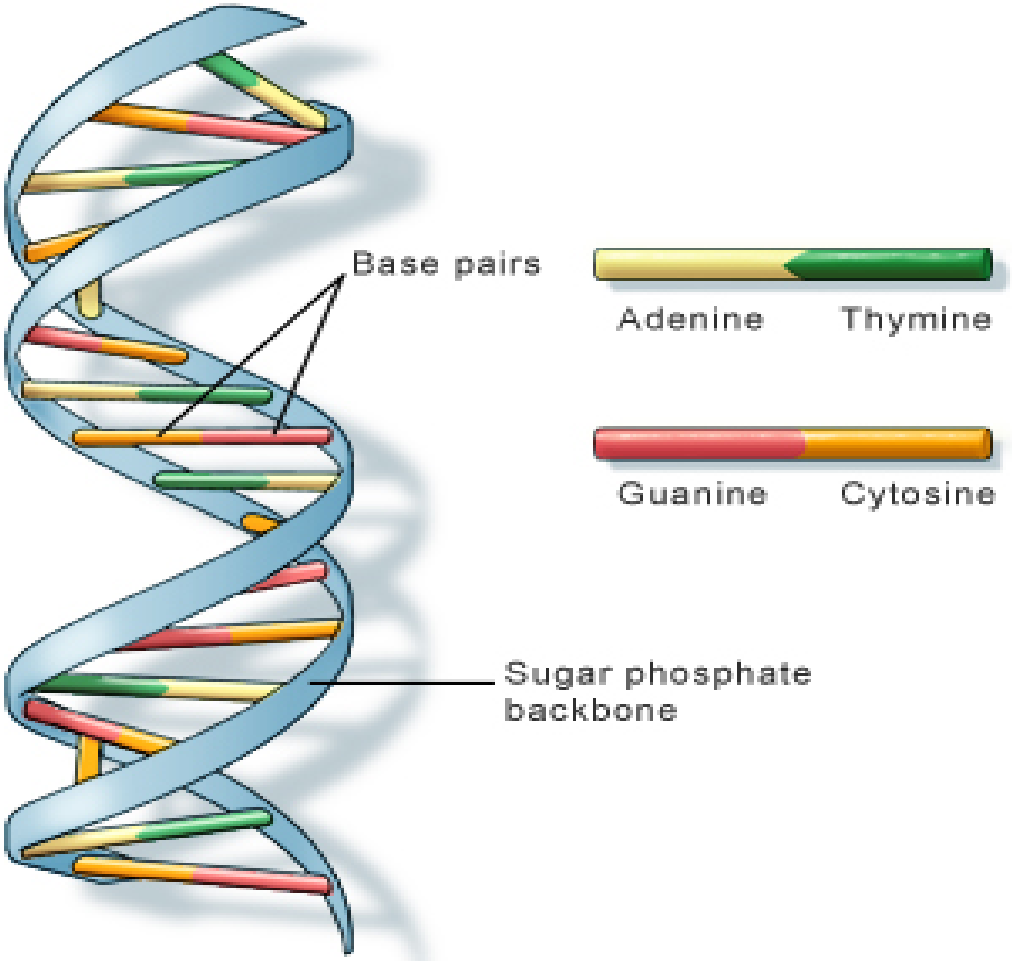
- The decision whether or not to undergo genetic testing may depend of several factors such as wanting to know if a client could pass the gene for a certain condition on to their offspring. Other clients may want to know if they carry a mutated gene, which would put them at risk for a certain condition.

Ethical, Legal, and Social Implications (ELSIs) of Genetic Testing

- Cultural, ethnic, and religious differences also have a significant affect on decisions about genetic testing.
- Morally, are individuals obligated to inform extended family members about inherited health risks?
- Some types of genetic testing are expensive and may not be covered by insurance. So…who gets the test? Those who can afford to pay for the test.

No DNA Test Necessary…

Review of DNA Make-up



Genes & Chromosomes

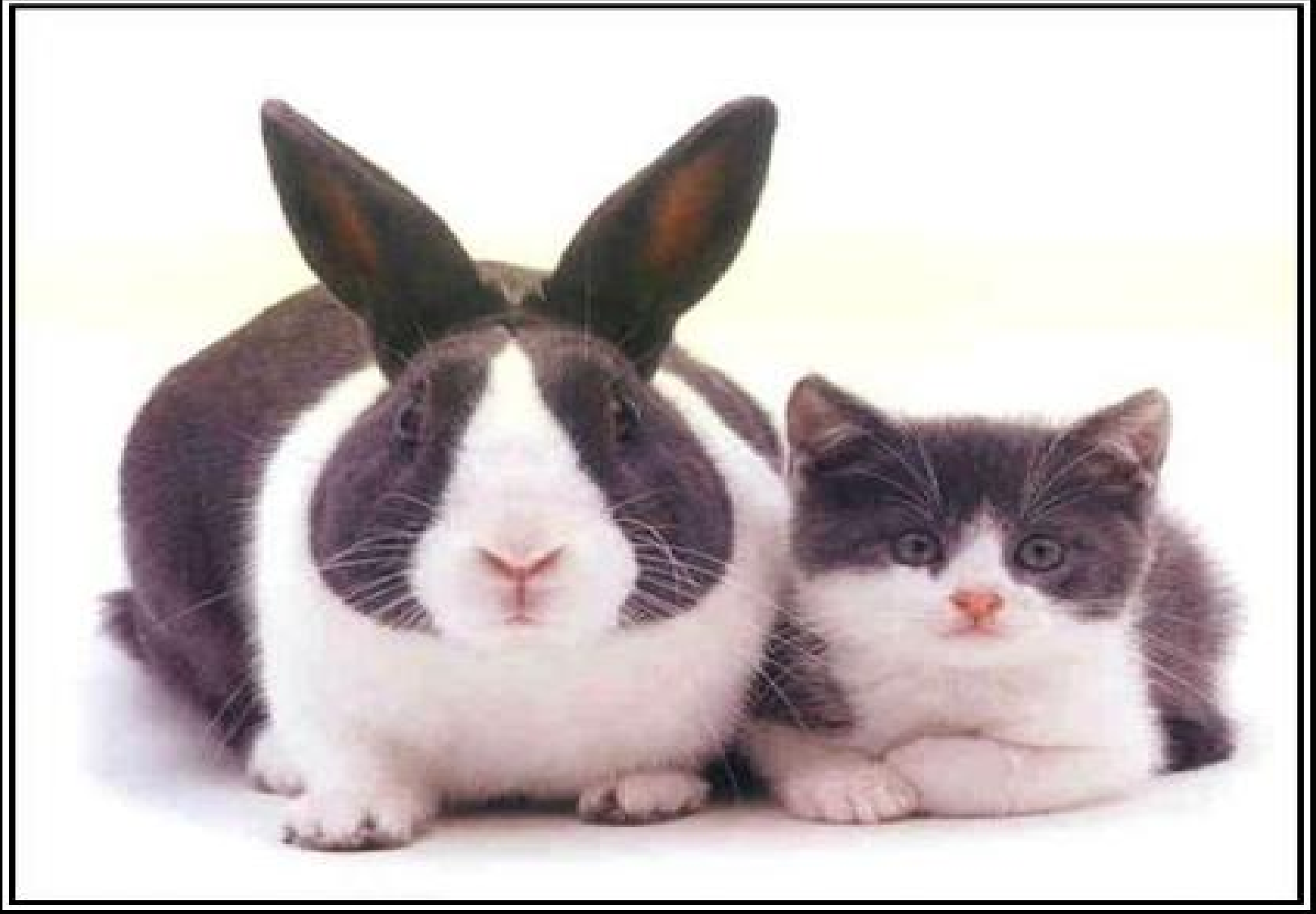
- **Chromosomes** - threadlike strands of DNA

- **Genes** – Chromosomes that are composed of many smaller segments of DNA. Genes contain coded information that determines and individual's unique characteristics.

  They never act in isolation; they always interact with other genes and the environment.

Cloning

- Reproductive cloning
- Therapeutic cloning
- Gene therapy
- Risks of cloning
  - Expensive & highly inefficient
  - Unstable genes (defects or mutations in the DNA) can cause problems
  - Offspring tend to have immune & growth problems



CLONING

Results may vary

Genes & Chromosomes

- All normal human somatic cells contain 46 chromosomes arranged as 23 pairs of homologous (matched) chromosomes.
- The 23 pairs are made up of one pair of sex chromosomes (X or Y) and 22 pairs of autosomes.
- Homologous chromosomes (except the X and Y chromosomes in males) have the same number and arrangement of genes. For example, the loci, or location on the chromosome, will contain both inherited pairs of genes for the same trait, such as eye color.

Genes & Chromosomes

- **Alleles** – these are genes at corresponding loci on homologous chromosomes that code for different forms or variations of the same trait. An individual having 2 copies of the *same* allele for a given trait is said to be **homozygous** for that trait; if there are 2 *different* alleles present, the person is **heterozygous** for the trait.

- Examples:
  - **Homozygous:** Brown eyes allele & another brown eyes allele
  - **Heterozygous:** Brown eyes allele & a blue eyes allele

HETEROZYGOATS

Just allele uneven.

Genes & Chromosomes

- **Genotype** – the genetic makeup of an individual &/or all the genes that the individual can pass on to future generations.

- **Phenotype** – the observable expression of an individual's genotype, such as physical features, a biochemical or molecular trait, or a psychologic trait.

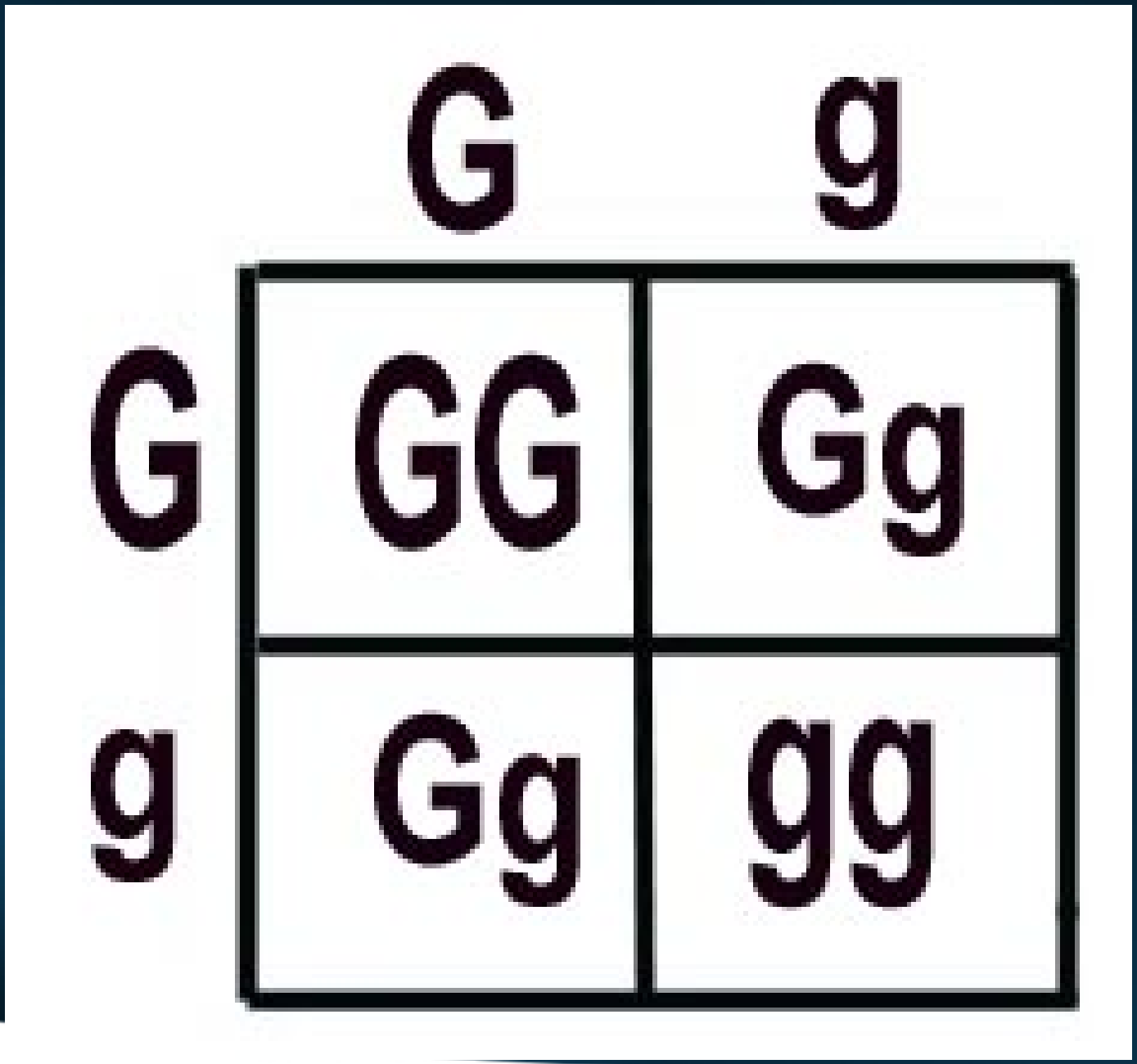
Genes & Chromosomes

- **Dominant trait or disorder** – it is expressed or phenotypically apparent when only one copy of the gene is present.

- **Recessive trait or disorder** – it is expressed or phenotypically apparent only if 2 copies of the gene are present.

Punnet Square

- Dominant disorders are capitalized (example: “T”)
- Recessive disorders are lower-case (example “t”)
- Each of the four boxes is worth 25% for a total of 100%
- Each % chance is for every pregnancy that the same couple produces (regardless of the couple’s previous pregnancies/children)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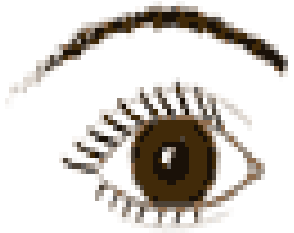


Mother
Bb

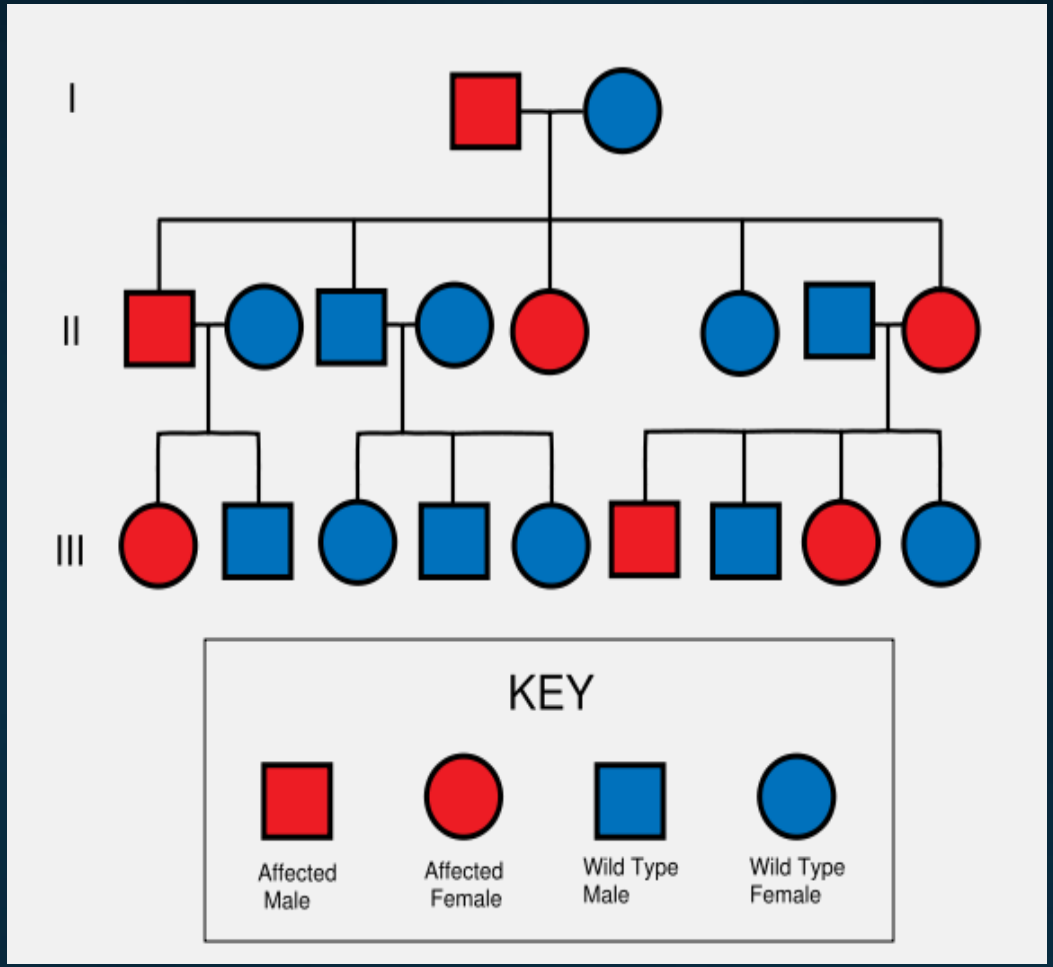
Father
Bb

BB	Bb
Bb	bb

Key: B = brown eyes
b = blue eyes

Pedigree

- Drawing a family history (pedigree) chart is a helpful shorthand method of in documenting affected relatives, identifying patterns of inheritance in families, and identifying those at risk for genetic conditions.



Factors to consider when using a pedigree or Punnet square

- Is the trait located on a sex chromosome or an autosome?
  - Autosomal (not on a sex chromosome)
  - Sex linkage (located on one of the sex chromosomes – either the X or the Y)

- How is the trait expressed?
  - Dominant (the trait is expressed in every generation)
  - Recessive (expression of the trait may skip generations – requires 2 traits to show up)

Genes & Chromosomes

- **Karyotype** – the pictorial analysis of the number, form, and size of an individual's chromosomes. The chromosomes are numbered from largest to smallest, 1 to 22 and the sex chromosomes (the 23 pair) are designated by the letter X or Y. A female karyotype is designated as 46, XX and a male karyotype is designated as 46, XY.

- Each chromosome is divided into two "arms" designated by a p (short arm) and q (long arm).

Sex Chromosome Abnormalities

- Several sex chromosome abnormalities are caused by nondisjunctions. The most common deviation in females is Turner Syndrome or monosomy X (45,X). The most common deviation in males is Klinefelter Syndrome or trisomy XXY.

Autosomal Dominant Inheritance

- Autosomal dominant disorders occur when only one copy of the abnormal gene is needed for phenotypic expression. The abnormal gene may appear as a result of a mutation, which is a spontaneous and permanent change in the normal gene structure.
  - Examples: heart disease, Marfan Syndrome, polycystic kidney disease, achondroplasia, and neurofibromatosis.

Autosomal Recessive Inheritance

- Autosomal recessive disorders occur when both genes of a pair must be abnormal for the disorder to be expressed. For the trait to be expressed, both carriers must contribute the abnormal gene to their offspring.
  - Examples: PKU, galactosemia, maple syrup disease, Tay-Sachs disease, sickle cell anemia, and cystic fibrosis.

Cancer & Genes

- Cancer is genetic in origin – one or more mutations make cells unstable.

- 3 classes of genes lead to cancer if they are mutated:
  - Protooncogenes/Oncogenes (promote normal G & D)
  - Tumor suppressor genes (halt or slow cell growth & division – prevent development of tumors)
  - DNA damage-recognition-and-repair genes (hunt down mutations and attempt to repair them)

Cancer & Genes

- People acquire mutations in genes in 3 ways:
  - Environment (ultraviolet light = skin cancer, tobacco smoke = lung cancer)
  - Heredity (we can be born w/ specific mutations)
  - Chance (normal metabolic processes can generate chemicals that damage DNA)

Genetic Counseling

- Typically provided by a team of genetics specialists: physician, medical geneticists with a PhD, genetics fellows, genetics counselors, &/or advanced practice genetics nurse specialists.
- Individuals and families seek out or are referred for genetic counseling for a variety of reasons and at all stages of their lives.
- They are given an occurrence or recurrence risk.
- Stick by the principle of nondirectiveness
- Your job is to know when a client needs to be referred for genetic counseling.

GENETICS

This is how it works

Down Syndrome

- 92% of the time, DS is caused by the presence of an extra chromosome 21 in all cells of the individual. At conception, the fertilized egg contains 3, rather than 2, 21st chromosomes. Thus, three copies of chromosome 21 are present – trisomy 21. There are 2 other genetic abnormalities that cause DS, mosaic trisomy 21 & translocation trisomy 21 – these are rarely the cause.
- Link to Alzheimer's Dx

Down Syndrome

- Maternal age can play a large role in the risk of DS – the older the female, the older her eggs are, the higher risk of DS. However, of the total population, older moms have fewer babies; about 75% of DS babies are born to younger women b/c more younger women than older women have babies.

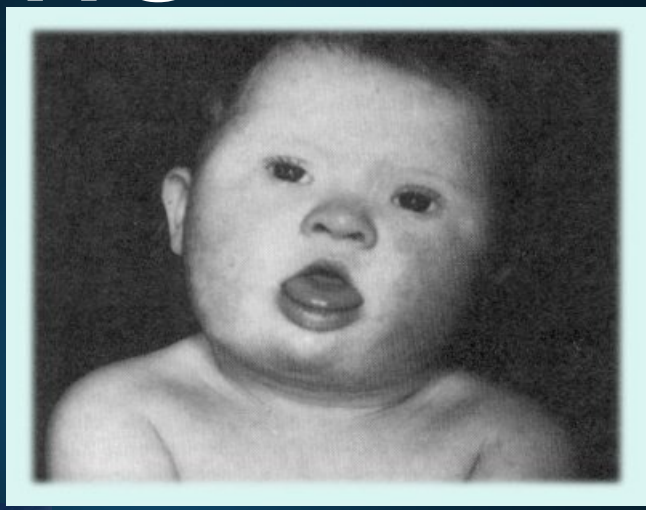
Down Syndrome: Clinical Phenotype

- Flat facial profile
- Upward eye slant with epicanthal fold
- Abnormally shaped, low-set ears
- Brushfield spots
- Simean crease on palms
- Hypotonia
- Protruding tongue
- Separated sutures at birth
- Short fingers, space b/t large & 2nd toe
- Microcephaly
- Hypothyroidism
- Hearing loss
- Vision problems
- **Congenital heart disease/anomalies**
- Constipation
- Atlantoaxial instability
- More likely to have chronic resp & ear infections
- Mental retardation
- GI abnormalities
- Increased risk of ALL

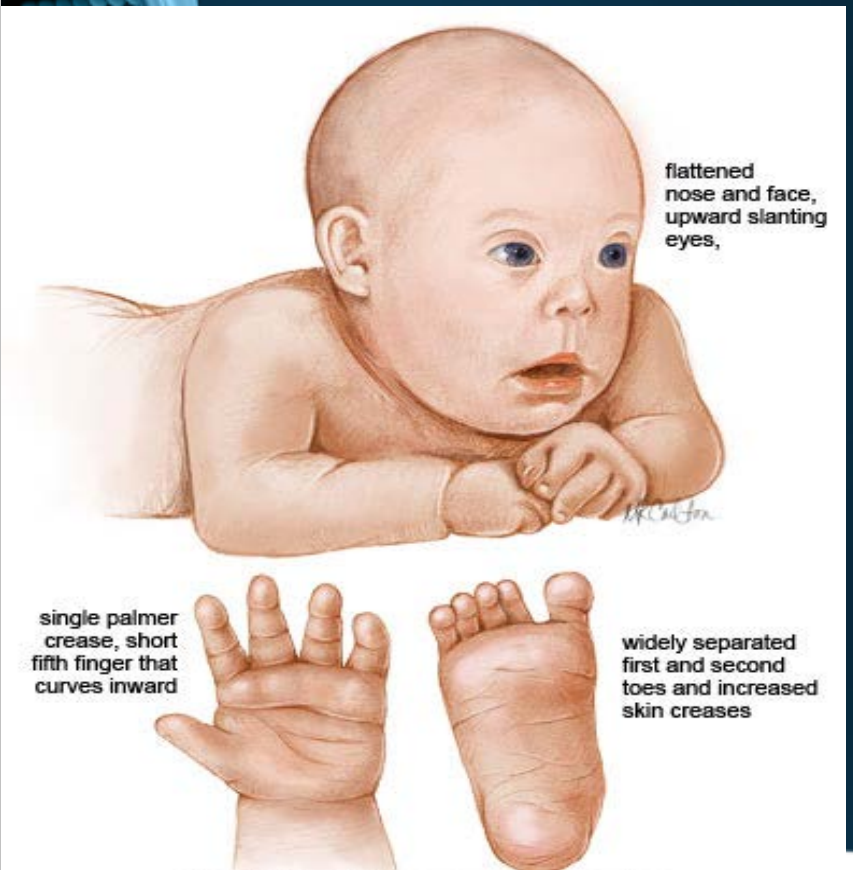
The risk of Down syndrome increases with the mother's age:

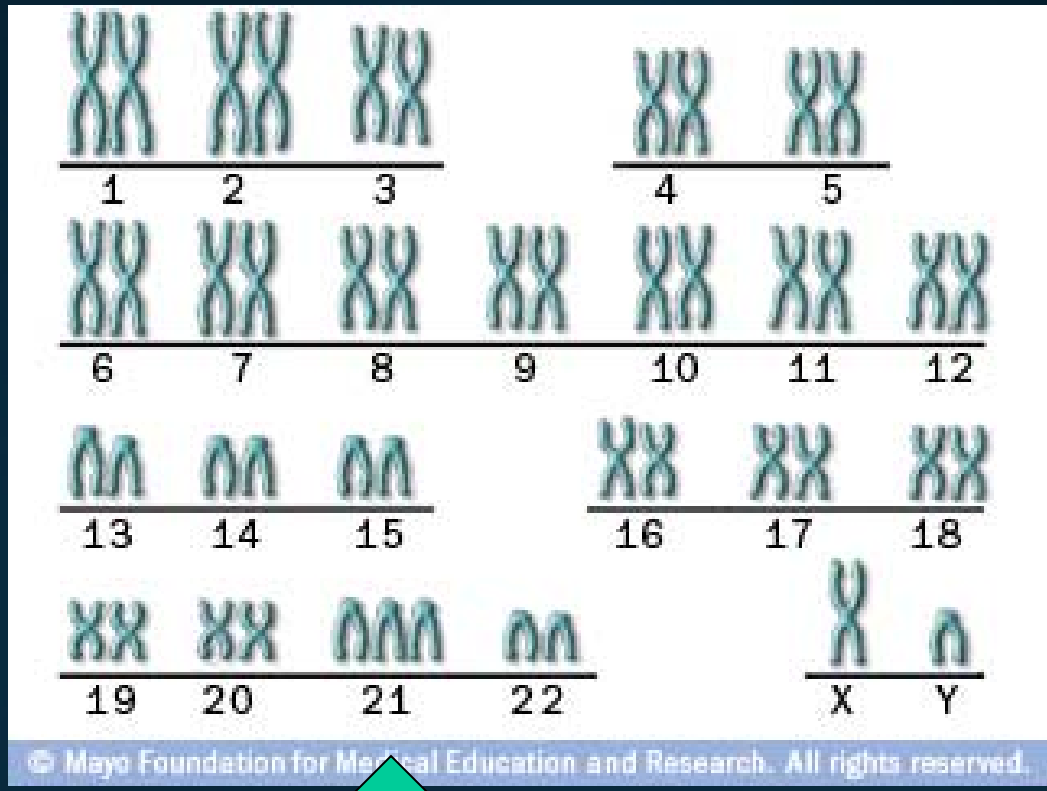
- At age 25, the risk of having a baby with Down syndrome is 1 in 1,250.
- At age 30, the risk is 1 in 1,000.
- At age 35, the risk is 1 in 400.
- At age 40, the risk is 1 in 100.
- At age 45, the risk is 1 in 30.

Down Syndrome



Down Syndrome

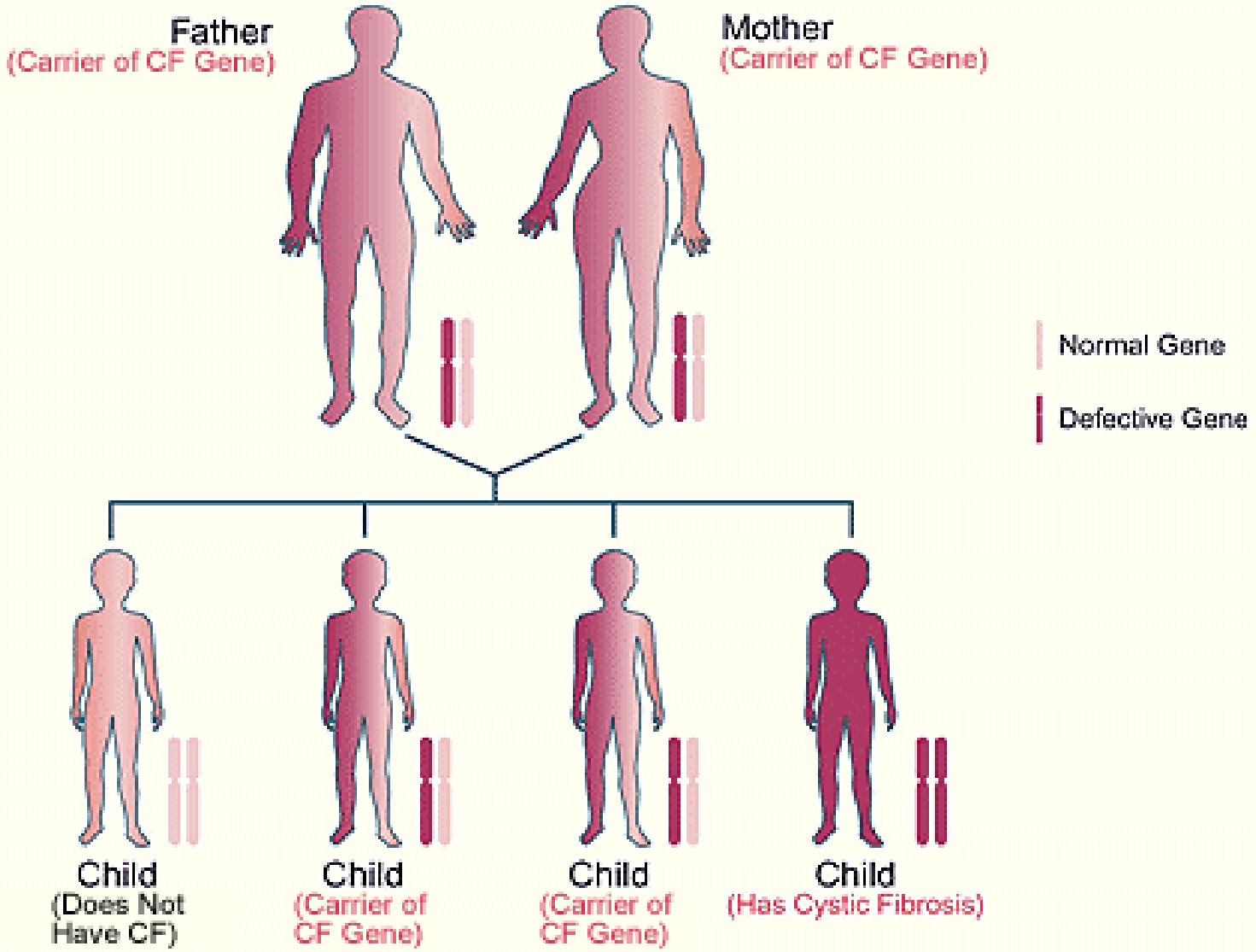




Cystic Fibrosis

- Auto-recessive disease
- About 40% of kids with CF live beyond age 18. Avg life span is 30-33 years.
- This disease affects sodium channels (mucus & sweat glands) in the body causing respiratory and digestive problems. Thick mucus is formed in the resp passages. Also, pancreatic enzymes that aid in the breakdown and absorption of fats in the intestine are absent, causing malabsorption and malnutrition.

Inheritance of Cystic Fibrosis (CF)



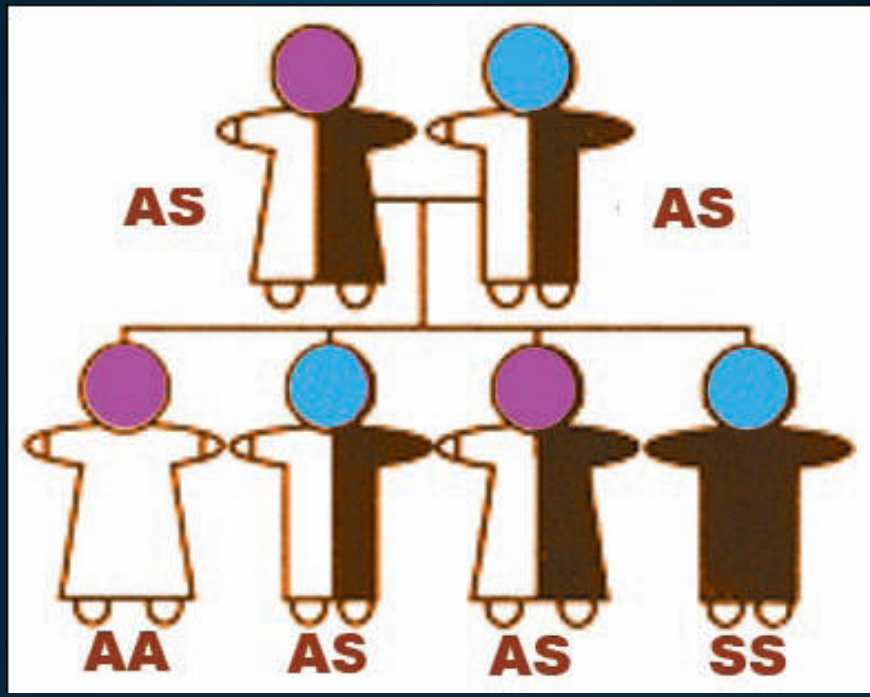
Cystic Fibrosis: Clinical Phenotype

- No meconium in first 48 hours after birth
- Stools are pale or clay colored, foul smelling, and they float
- Skin may taste salty
- Recurrent resp inf, esp pneumonia & sinusitis
- Coughing or wheezing
- Wt loss
- Diarrhea
- Delayed growth
- Fatigues easily
- Watch for rectal prolapse
- Later, watch for clubbing, barrel chest, cyanosis

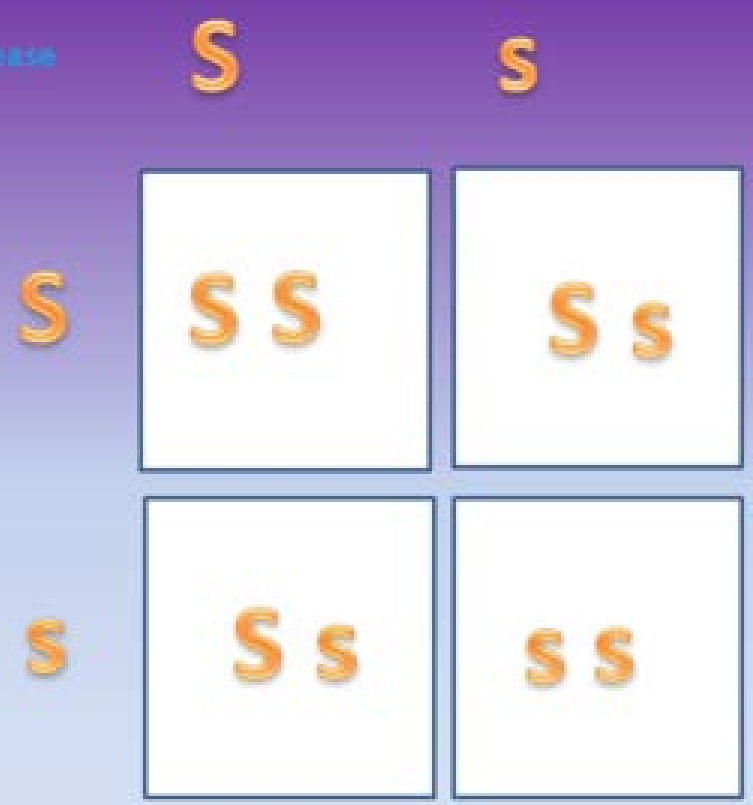
Sickle Cell Anemia

- Autosomal recessive disorder
- RBCs are sickle (or crescent) shaped instead of the normal disc shape.
- Normal Hgb A is replaced partly or completely by abnormal Hgb S
- Kids who inherit Hgb A from one parent & Hgb S from the other will only carry the trait – they will have only mild or no symptoms
- Most common in African Americans – has been noted in Hispanics and Whites (especially of Mediterranean descent). 1 in 12 African Americans carry the trait.

Sickle Cell Anemia

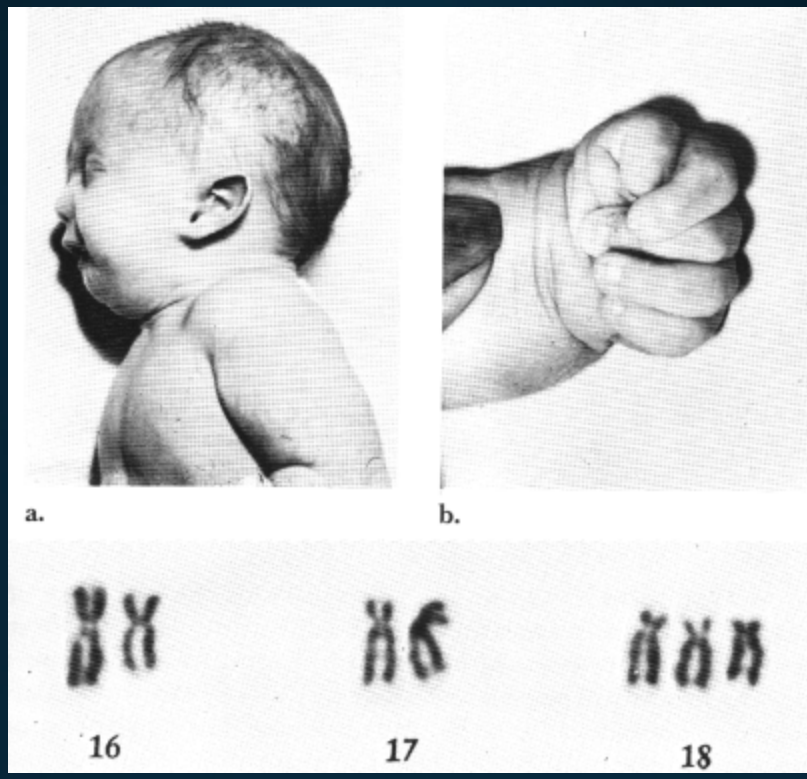


Key:
SS: Doesn't have disease
Ss: Carrier
ss: Affected



Edward Syndrome (Trisomy 18)

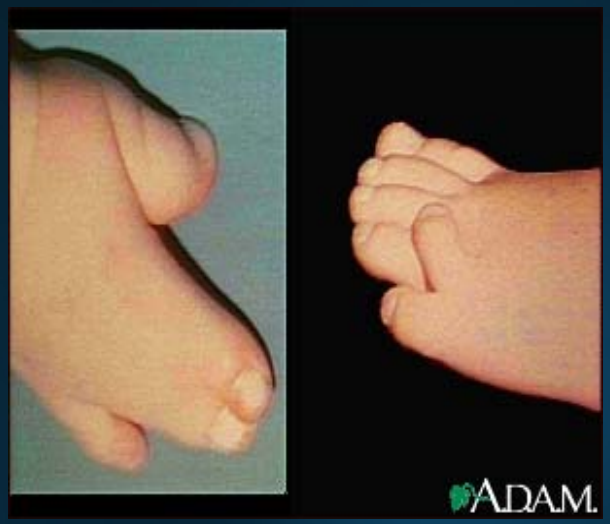
- Presence of a third number 18 chromosome
- Many of the abnormalities are not compatible with life beyond 1 year
- Pregnant females whose fetus has this disease may show extra amniotic fluid (polyhydraminos), enlarged uterus, and a small placenta.

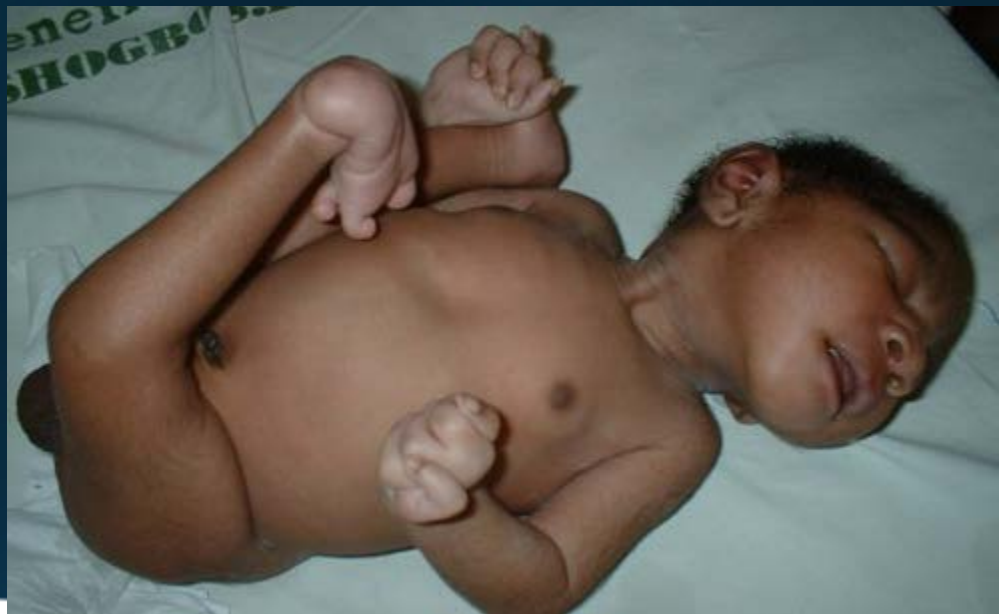


Edward Syndrome (Trisomy 18): Phenotype

- LBW infant
- Mental deficiency
- Low-set malformed ears
- Small jaw (micrognathia)
- Clenched hands; hand abnormalities; index finger overlaps third finger
- Rocker-bottom feet
- Crossed legs (preferred position)
- Kidney & genital abnormalities
- Microcephaly
- Short sternum
- Mental retardation
- Hernias
- Undescended testicles
- Congenital heart disease

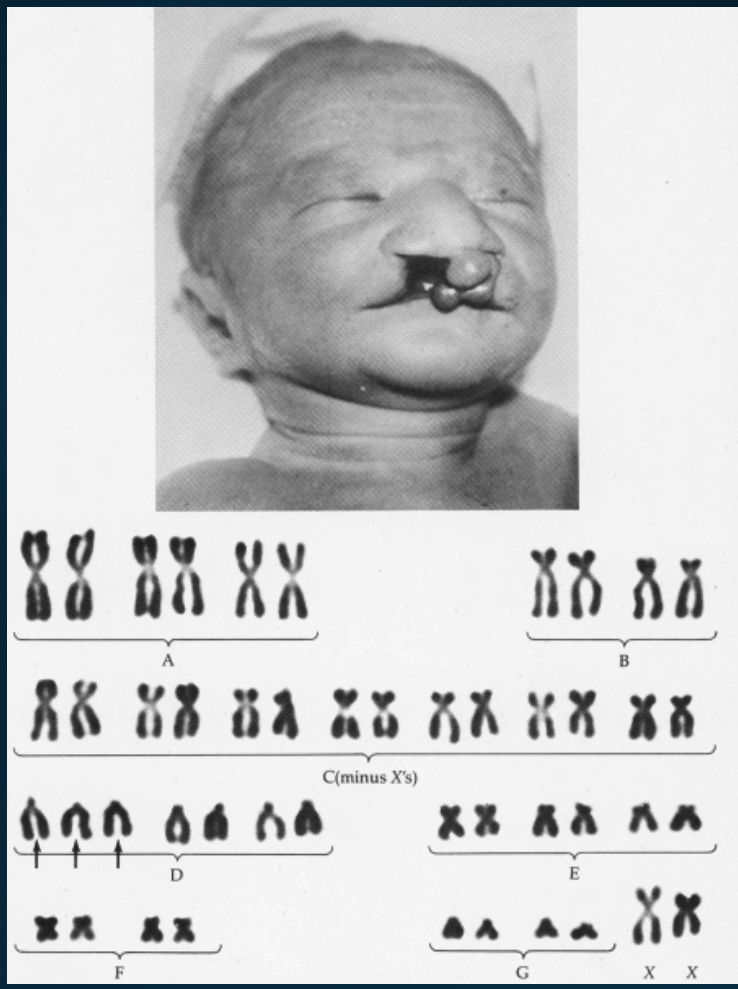
Edward Syndrome (Trisomy 18)





Patau Syndrome (Trisomy 13)

- Presence of a third number 13 chromosome
- Due to the severe abnormalities, many which are not compatible with life, almost ½ do not survive beyond the first month and ~ ¾ die within 6 months
- At birth, the infant may have a single umbilical artery and s/s of congenital heart disease. The infant may have abnormal rotation of the internal organs. The brain's cerebral hemispheres are fused.



Patau Syndrome (Trisomy 13)

- Severe mental retardation
- Seizure activity
- Small head (microcephaly)
- Scalp defects (triplet areas of aplasia cutis congenita)
- Small eyes (microphthlamia)
- Cleft lip/palate
- Eyes closely set, may be fused into one
- Iris defects
- Low-set, abnormally shaped ears
- Simian crease
- Extra digits (polydactyly)
- Hernias
- Undescended testicle (crytorchidism)
- Hypotonia
- Micrognathia
- Skeletal abnormalities
- Abn heart placement
- Heart defects

Patau Syndrome (Trisomy 13)

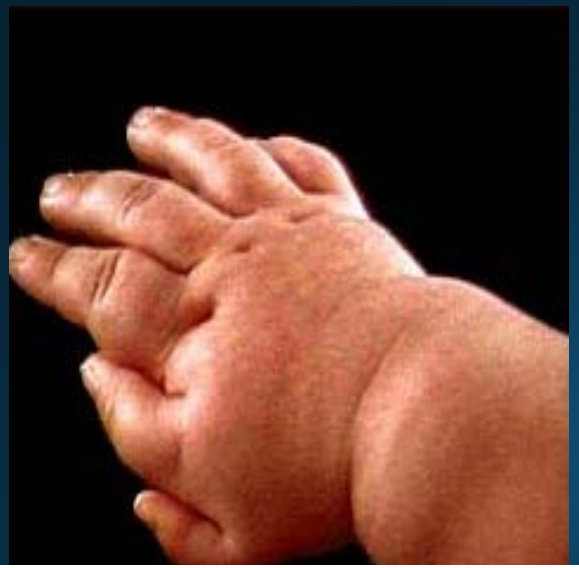


Figure 2. The Patau syndrome patient at 28 months.

Turner Syndrome

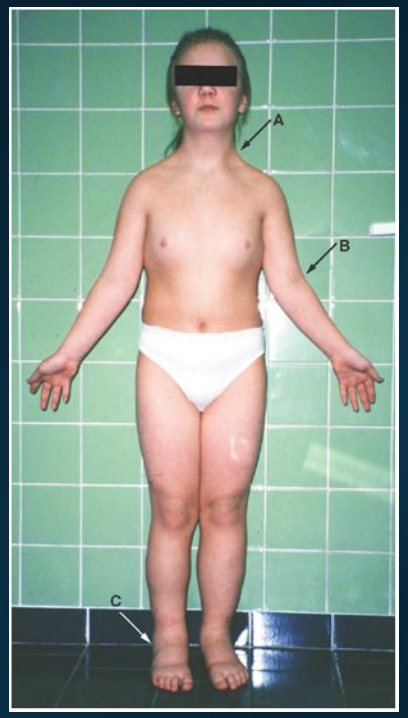
- Sex chromosome disorder caused by lack of an X chromosome (45,X); thus only females can have this
- Will have underdevelopment of the uterus, vagina, ovaries, and breasts. Will be short-stature (usually no taller that 5 ft). Usually not mentally retarded but can be slow to learn. Can have kidney problems, HTN, and congenital heart defects.
- Early s/s: puffiness of hands and feet at birth, webbed neck with low hairline, short 4th fingers, inability to fully extend elbows, pigmented mole-like skin lesions

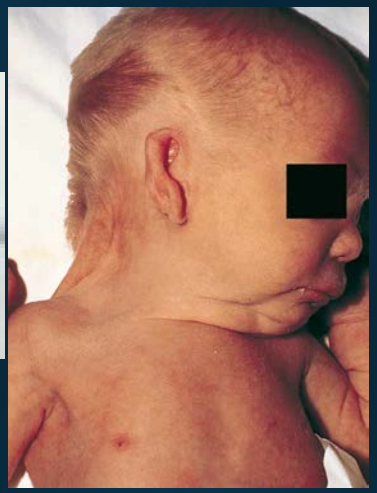
Turner Syndrome: Phenotype

- Puffiness of hands & feet at birth
- Webbed neck with low hairline
- Short 4th finger
- Inability to fully extend elbows
- Pigmented mole-like skin lesions
- Short stature
- Possible kidney & heart defects
- Simean crease
- Abn eye features, like droopy lids & dry eyes
- Abn bone dev, such as a “shield-shaped” broad flat chest – widely spaced nipples
- Absence or underdeveloped secondary sexual characteristics – absent menstruation, absence of normal moisture in vagina = painful intercourse
- Infertility

Turner Syndrome

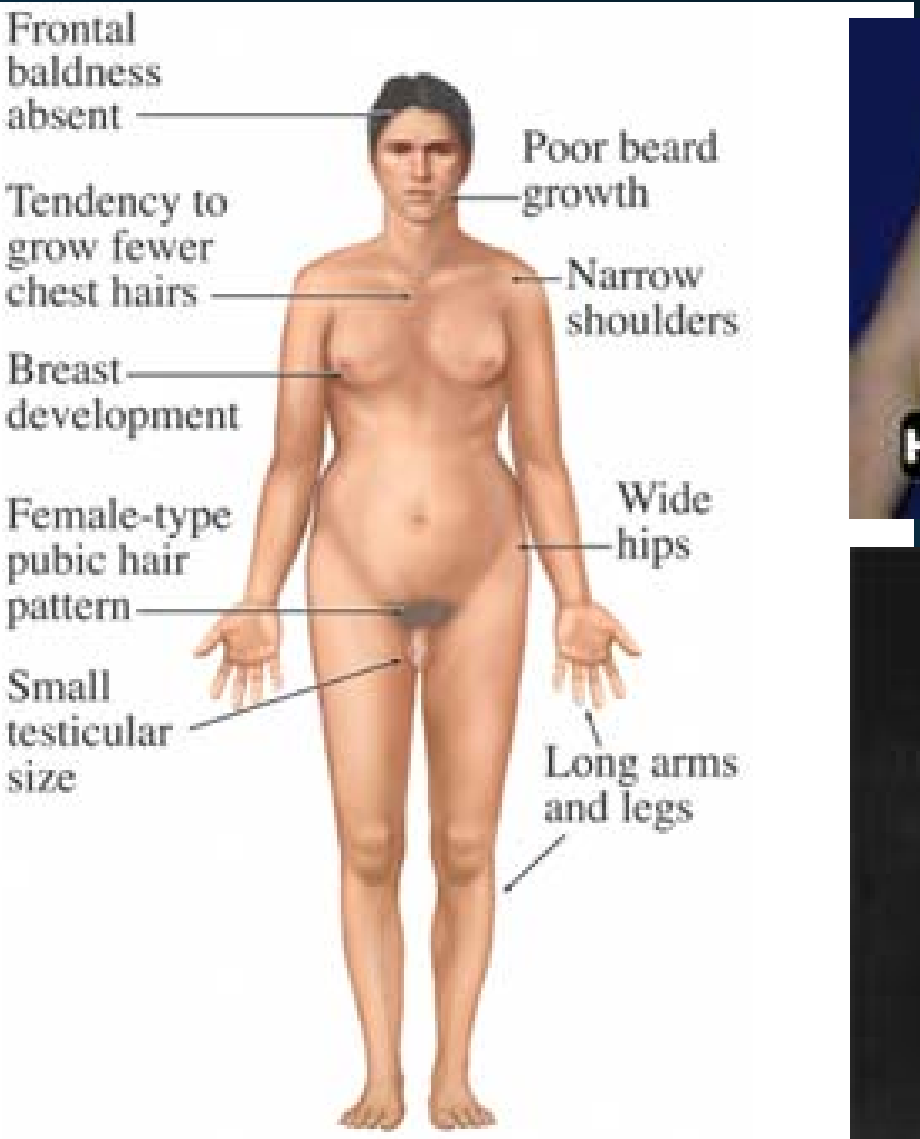
- Females are usually infertile
- Tx: growth hormone, estrogen, anabolic steroids
- At risk for: diabetes, thyroid disorders



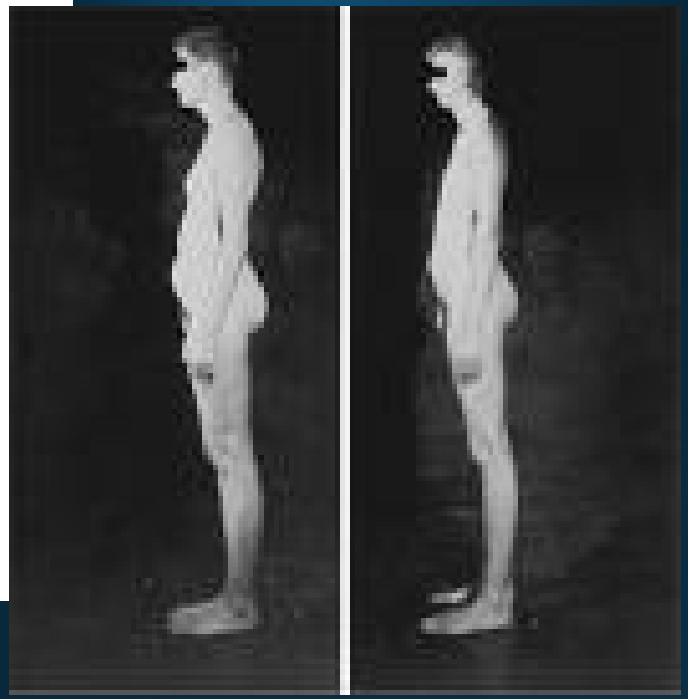


Klinefelter Syndrome

- Syndrome caused by the presence of one or more additional X chromosomes – the majority of males with this syndrome are 47, XXY. The severity of the phenotype depends on how many X chromosomes they have.
- Fairly common: 1 in 500 – 850 men
- Usually diagnosed in puberty when secondary sexual characteristics fail to develop (or develop late). The majority of these men are infertile.
- This is not inherited; one main risk factor is an older aged mom.


Frontal baldness absent
Poor beard growth
Tendency to grow fewer chest hairs
Narrow shoulders
Breast development
Female-type pubic hair pattern
Wide hips
Small testicular size
Long arms and legs

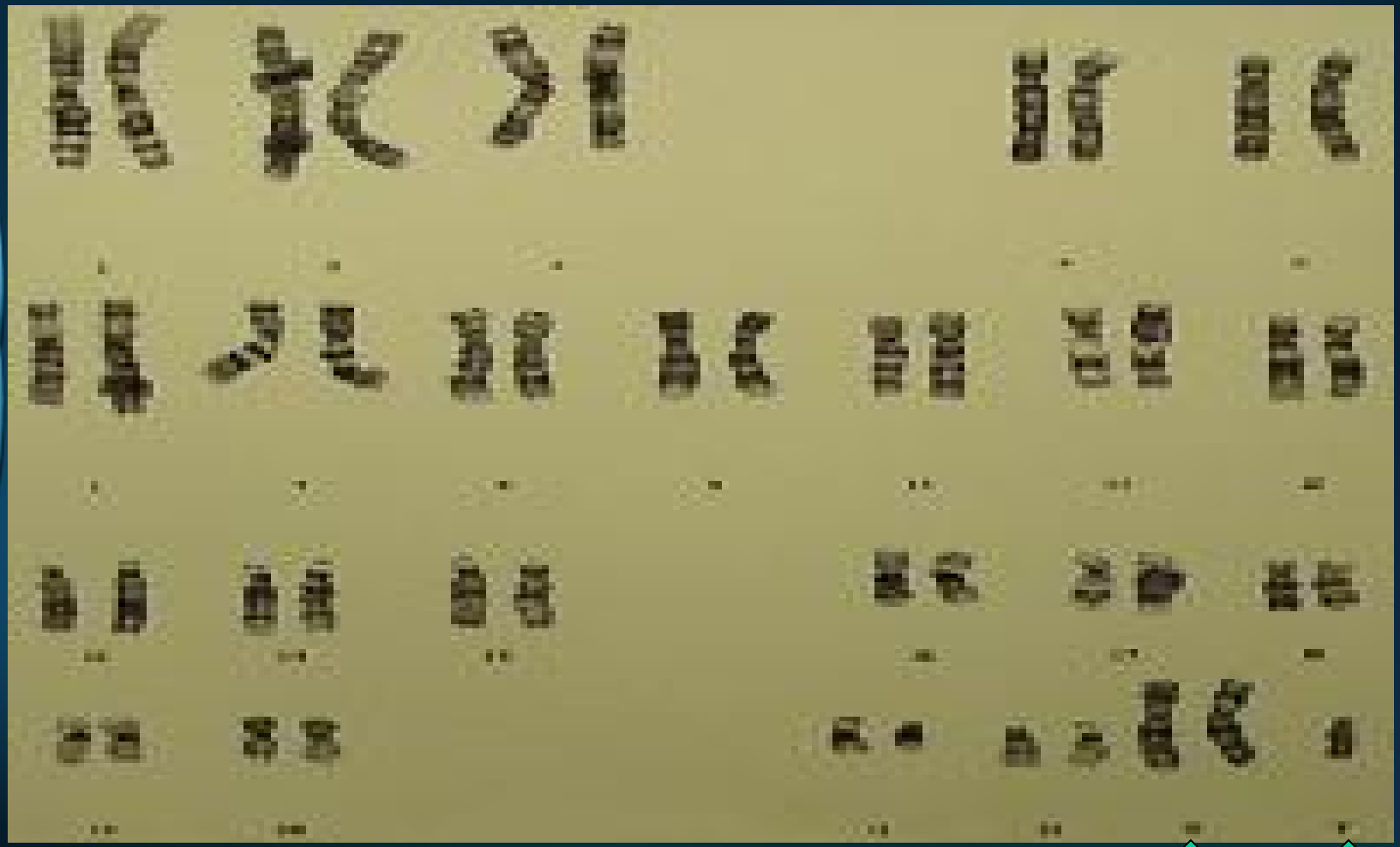

HSL



Klinefelter Syndrome: Phenotype

- Tall stature with abn body proportions (long legs, short trunk)
- Small penis with small firm testicles or one testicle
- Diminished pubic, axillary, & facial hair
- Sexual dysfunction
- Enlarged breast tissue (gynecomastia)
- Learning disabilities, despite normal or high IQ Level (poor verbal skills & auditory memory)
- Increased risk for dyslexia and ADHD
- Enlargement of the pulp of the teeth (taurodontism)
- Behavioral problems (shyness, passivity, aggression)

Klinefelter Syndrome



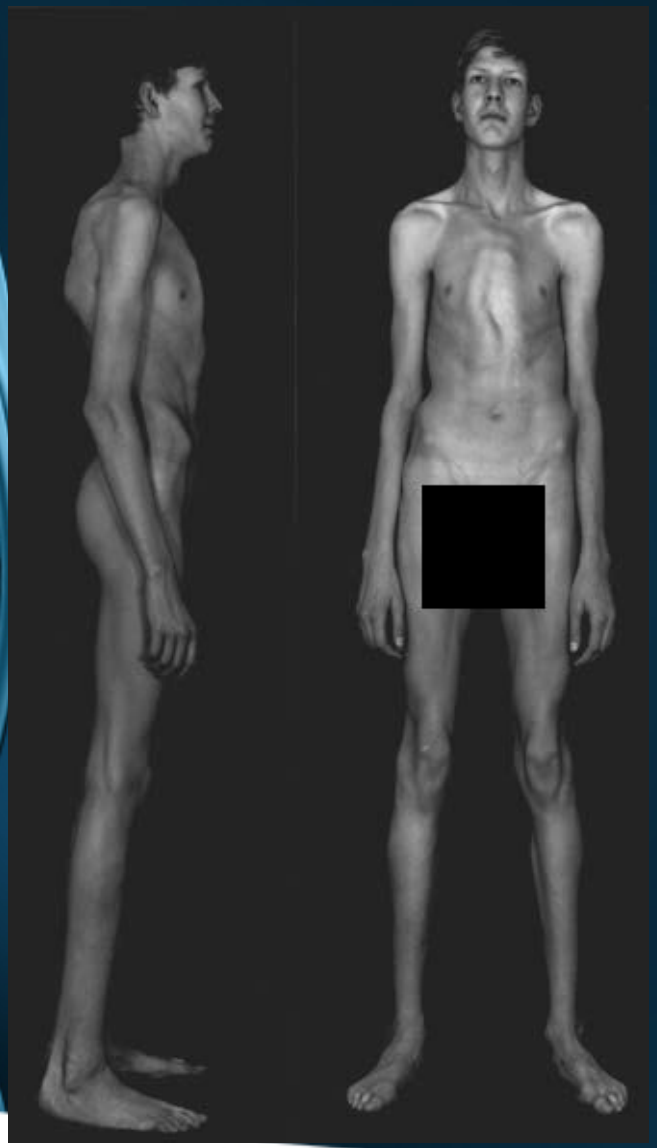
Marfan Syndrome

- Autosomal dominant trait, can occur without a family hx though (mutation)
- This syndrome changes the body's elastic tissue, particularly in the aorta, eye, and skin. There is also overgrowth of the long bones, resulting in tall stature and long limbs.
- Life-threatening problems include CV abnormalities: development of a dissecting aortic aneurysm. Other problems are dilatation of the base of the aorta with aortic regurgitation & mitral valve prolapse.

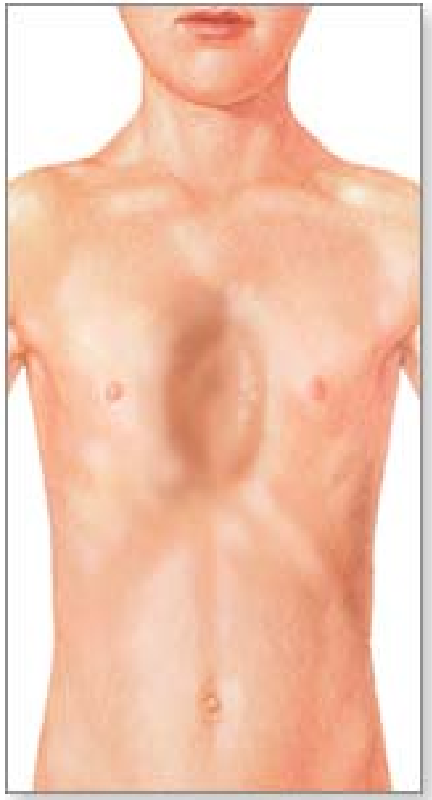
Marfan Syndrome: Phenotype

- Long, lanky frame with thin limbs
- Armspan is significantly greater than body ht
- Long spidery fingers (arachnodactyly)
- Funnel chest (pectus excavatum) or pigeon chest (pectus carinatum)
- Scoliosis
- Visual problems
- Thin, narrow face with a high arched palate and crowded teeth
- Hypotonia
- Micrognathia (small lower jaw)
- Learning disabilities/school problems
- Cardiac problems: dilated aortic root, aortic regurgitation, dissecting aortic aneurysm, mitral valve prolapse

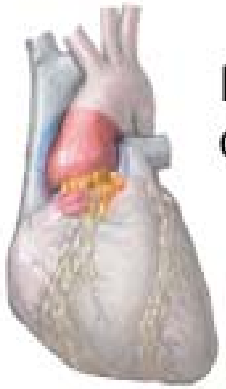
Marfan Syndrome



Pectus excavatum



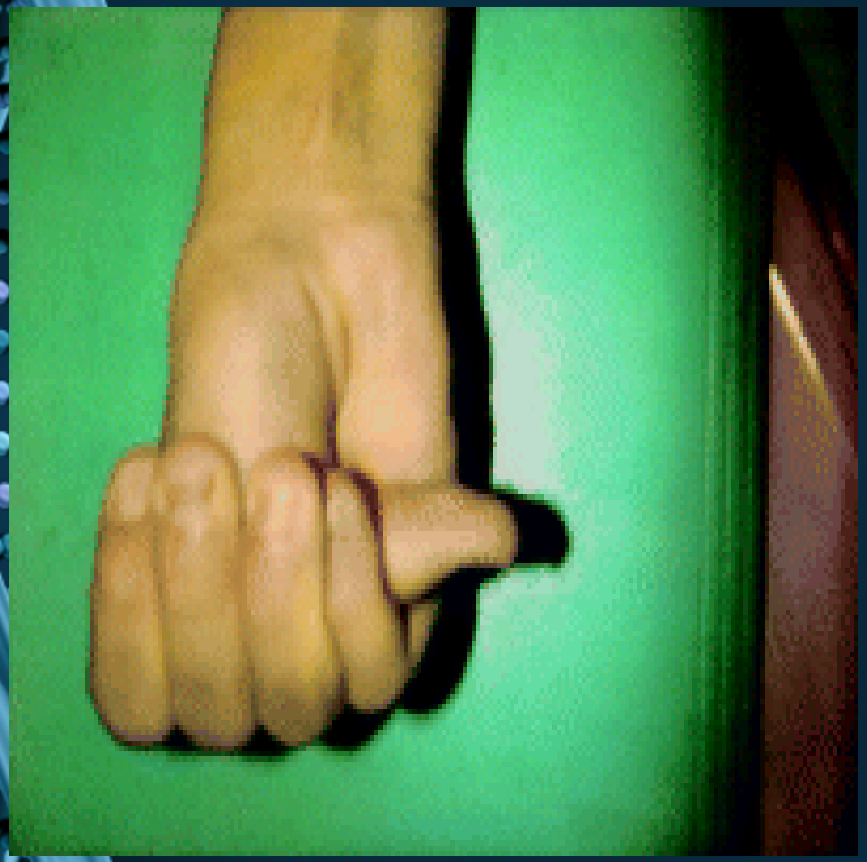
arachnodactyly

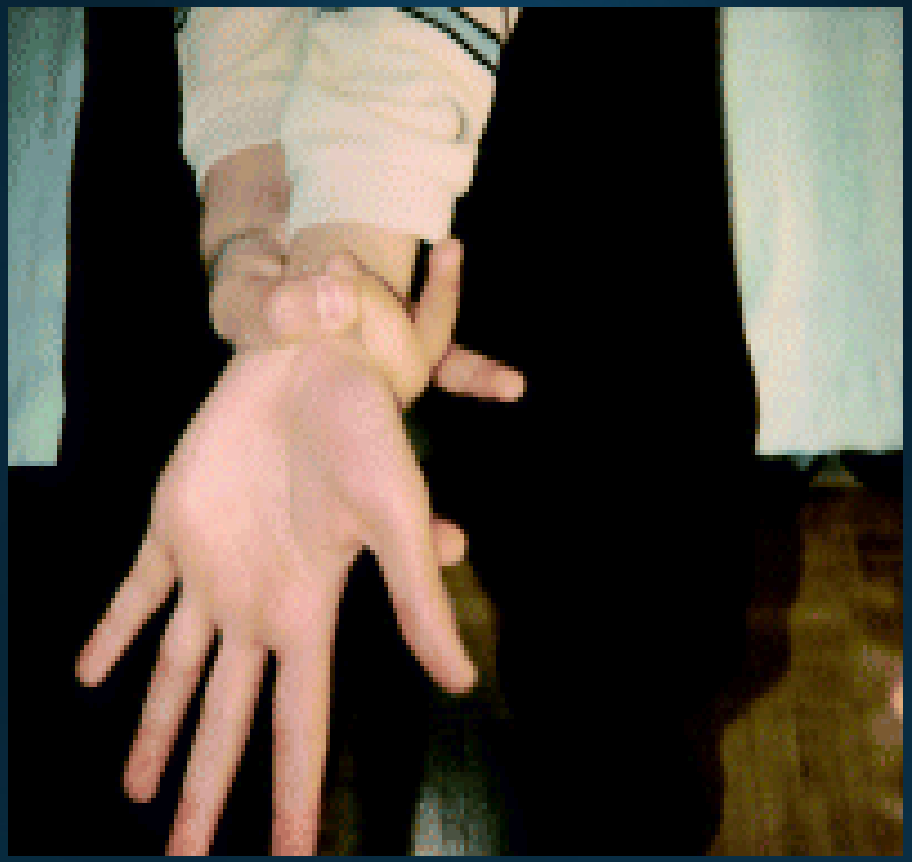


Dilation of aorta

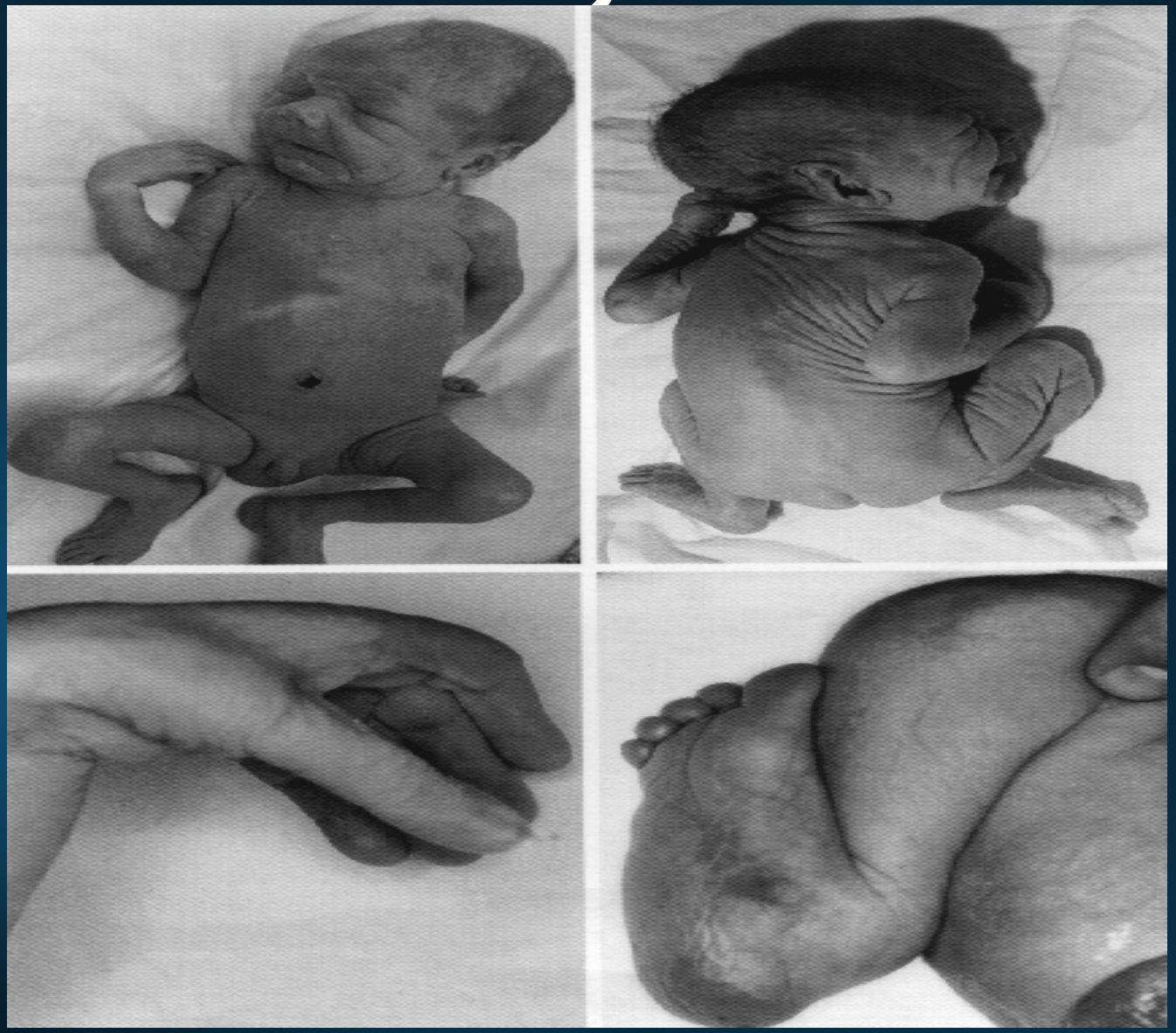
A.D.A.M.

Marfan Syndrome





Marfan Syndrome



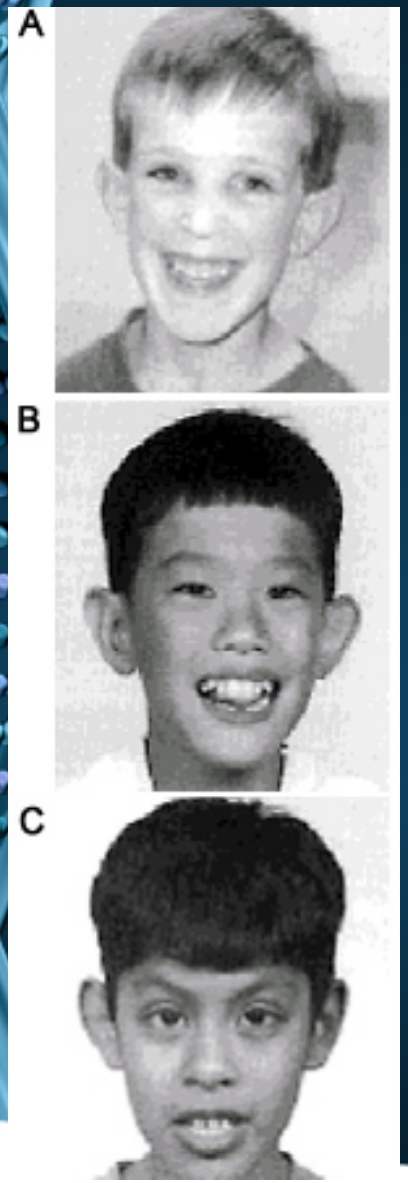
Fragile X Syndrome

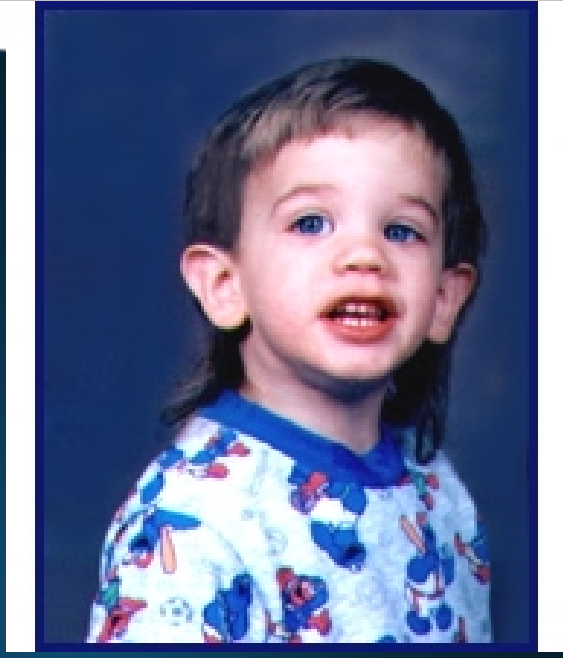
- Occurs from a fragile area on the X chromosome that tends to repeat bits of the genetic code; the more repeats, the more likely there is to be a problem.
- Most common form of inherited mental retardation in males & a significant cause in females.
- No treatment; effort is directed toward training and education so that affected children can function at maximal capacity.
- Family hx is a risk factor, especially a male relative

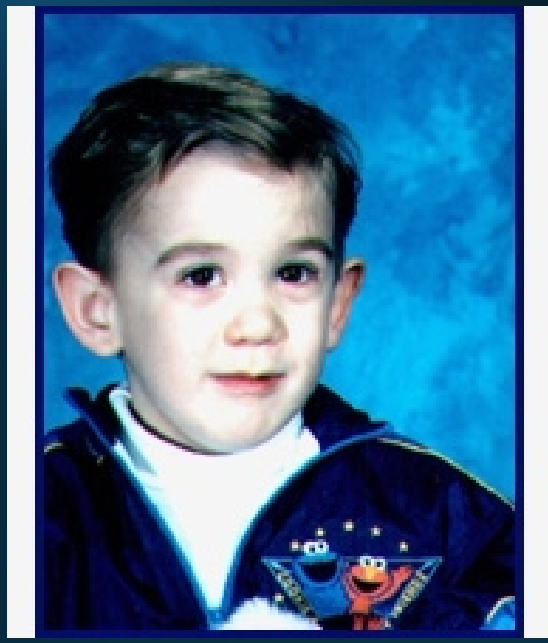
Fragile X Syndrome: Phenotype

- Mental retardation
- Large testicles (macro-orchidism)
- Large size
- Tendency to avoid eye contact
- Large forehead &/or a prominent jaw
- Babies tend to have a large head circumference
- Hyperactive behavior – can be aggressive

Fragile X Syndrome







Neurofibromatosis

- People with Neurofibromatosis are at least 5 years old with more than 6 light brown spots (cafe-au-lait spots) larger than 1.5 centimeters. They also have axillary freckles "Crowe's sign" and brown or skin colored nodules (neurofibromas) that are raised. Networks of nerve-cell tumors that are droopy, soft, doughy masses (plexiform neuromas) are also common.
- Autosomal dominant disorder that affects the bone, the nervous system, soft tissue, and the skin. Clinical manifestations increase over time.

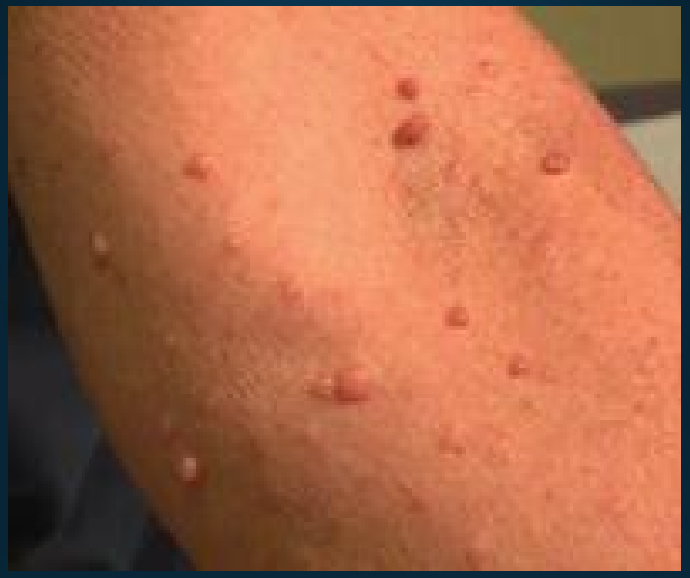
Neurofibromatosis

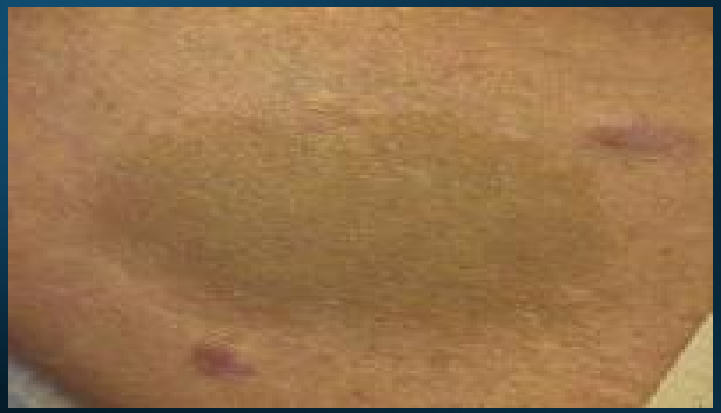
- Café au lait spots are irregularly shaped, evenly pigmented, brown macules. Most clients with Neurofibromatosis have 6 or more spots that are 1.5 cm or greater in diameter. In young children, be suspicious if there are 5 or more café au lait macules greater than 0.5 cm in diameter.
- Axillary freckling (as well as freckling on the perineum), known as the Crowe sign, often develop during puberty.
- May see bowing of the long bones &/or orbital defects.
- Many clients with this disease will have below average intelligence & short stature

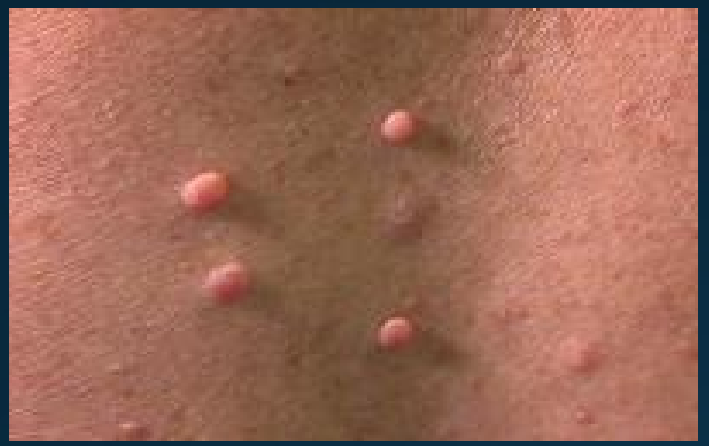
Neurofibromatosis

- Expect the client, esp if they are still being tested for this, to have an MRI to view the brain and soft tissues.
- A Wood lamp examination may be useful in patients with very pale skin in an effort to better view café au lait macules and for the eye examination.
- The client may have surgery to remove the macules if they become a problem, although they can grow back.

Neurofibromatosis







Huntington’s Chorea (Disease)

- Autosomal Dominant
- Huntington's disease results from genetically programmed progressive degeneration of brain neurons. This degeneration causes uncontrolled movements, loss of intellectual function, and emotional disturbance.
- S/S usually appear during middle age, but can appear younger (worse cases)
- Life expectancy is 10 - 20 yrs after onset

Future of Genetics in Healthcare

- Genetic testing can improve healthcare by predicting:
  - Sensitivity to certain drugs
  - Allergies
  - Behavioral difficulties
  - What therapies will likely be more successful for a specific disease
  - Identifying high-risk diseases
  - Identifying diseases that the patient is at a low-risk for

Integration of Genetic Services into Routine Patient Care

- Identify patients who would benefit from genetic counseling and/or testing
- Determine if clinical tests are available for a condition with a genetic component
- Provide genetic testing for disorders that are common in the population of Hawaii
- Identify laboratories that can provide testing for other genetic disorders
- Interpret test results so that the physician and/or patient can adequately understand them in order to make meaningful and helpful decisions regarding their healthcare

Genetic Testing Available to the Public

- 23andMe.com (https://www.23andme.com/) offers:
  - Genetic testing for over 40 inherited conditions (carrier status and disease risk)
  - Genetic testing to determine the effect of some common drugs (effectiveness of drug); i.e., Coumadin, Plavix, statin drugs
- Requires saliva (1/4 tsp) for testing
- Cost: $99.00

- Counsyl Testing offers similiar testing https://www.counsyl.com/diseases/

"Here's your sonogram. It's a girl, her name is Chelsea, she has a talent for music and she hates broccoli."

Questions/Comments

References

Lowdermilk, D. & Perry, S. (March 2007). *Maternity & Women's Health Care*, (9th ed.). St. Louis, MO: Mosby Elsevier.

The Queen's Medical Center (2013, March 17). *Genetics: The future of medicine*. Retrieved from http://www.queensmedicalcenter.net/services/90-genetics-the-future-of-medicine